Long-term neurocognitive impairment after general anaesthesia in childhood: Is obstructive sleep apnoea to blame?

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EDITORIAL

Long-term neurocognitive impairment after general anaesthesia in childhood

Is obstructive sleep apnoea to blame?

Markus Weiss, Thomas Engelhardt and Tom G. Hansen

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For more than 2 decades, laboratory research has consistently demonstrated widespread neurodegeneration and persistent learning deficits in the developing animal brain following early exposure to common anaesthetic agents.[1] The biological plausibility – humans are an animal species – triggered hundreds of further laboratory studies to identify potential pathways and mechanisms for providing 'safe' anaesthesia drugs and treatments to prevent potential cerebral damage in humans.[2] Given that anaesthesia is provided worldwide to several million children every year, a heightened interest in anaesthesia and public fear, as well as unease and uncertainty amongst professionals, has ensued. This has led to a US Food and Drug Administration (FDA) warning for the use of general anaesthetics in children younger than 3 years of age.[3]

Meanwhile, two prospective clinical trials and several large-scale retrospective cohort studies have shown that a single exposure to anaesthesia in early childhood does not significantly affect neurocognitive development.[4–7] Three further large-scale cohort studies reported that children who had undergone surgery at the age of 2 to 4 years, had an increased likelihood of early developmental impairment compared with unexposed children. Younger children were not affected.[8–10] In addition, multiple anaesthetic exposures in these children had no effect on the risk of early developmental impairment.[9,10]

Approximately one-third of the overall general anaesthesia workload in children of preschool age are ear-nose-and throat (ENT) problems,[11] with a large but variable proportion undergoing adeno and/or tonsillectomy between 2 and 4 years of age.[12,13] The principal indication for the surgical removal of hyperplastic tonsillar tissue at this stage of life is obstructive sleep apnoea syndrome (OSAS), which arises from episodic pharyngeal airway obstruction of airflow during sleep and associated nocturnal hypoxaemia, hypercarbia, sleep fragmentation and arousals from sleep.[13,14] Children with OSAS have long been identified as being at risk of 'backwardness and stupidity'.[15] There is now further evidence that OSAS in early childhood leads to impairment of behavioural and neurocognitive function and early treatment of paediatric OSAS may improve a child's long-term cognitive, social potential and school performance.[16–18] Furthermore, children who suffer from OSAS also commonly experience hearing problems and infections affecting speech and development. In addition, children undergoing ENT-procedures have a higher risk of anaesthesia-related critical incidents, and in those with OSAS, the risk may be even higher.[19,20] They experience an increased rate of apnoea and hypoxaemia, especially when they are treated with opioids and insufficiently monitored postoperatively after adeno/tonsillectomy. This may lead to hypoxic neurologic injury and in some cases even death.[13,21,22]

MRI has demonstrated changes in regional brain tissue integrity and alteration in regional brain thickness in these patients with OSAS,[23,24] although the latter findings have also (spuriously) been linked to exposure to general anaesthesia in these children.[25] MRI changes in young children with OSAS are thought to be due to a range of acute processes, including repeated arousals, hypoxia and re-oxygenation and episodic hypercarbia.[26] Intermittent hypoxia during sleep demonstrates

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intermittent substantial deterioration of behavioural performance with parallel disruption of the anatomical substrate (cell death) in an animal model.[27] However, these early laboratory findings have not had the same publicity as laboratory studies on anaesthesia drug-related neuroapoptosis, although the existing clinical evidence is readily available, and untreated OSAS undoubtedly has a huge impact on the neurocognitive development and general health of preschool children.[3,15]

The increased peri-operative risk for anaesthesia-related respiratory complications, together with OSAS-related neurocognitive and behavioural impairments in these children, may represent a key explanation for the repeated findings of neurocognitive impairment after anaesthesia among preschool children and must be considered in future studies investigating the effect of anaesthetics on neurocognitive and behavioural outcome. Rather than avoiding elective paediatric surgery with general anaesthesia below the age of 3 years, preschool children with suspected OSAS should be operated on earlier and treated in specialist hospitals providing high-quality peri-operative care.[19,28]

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